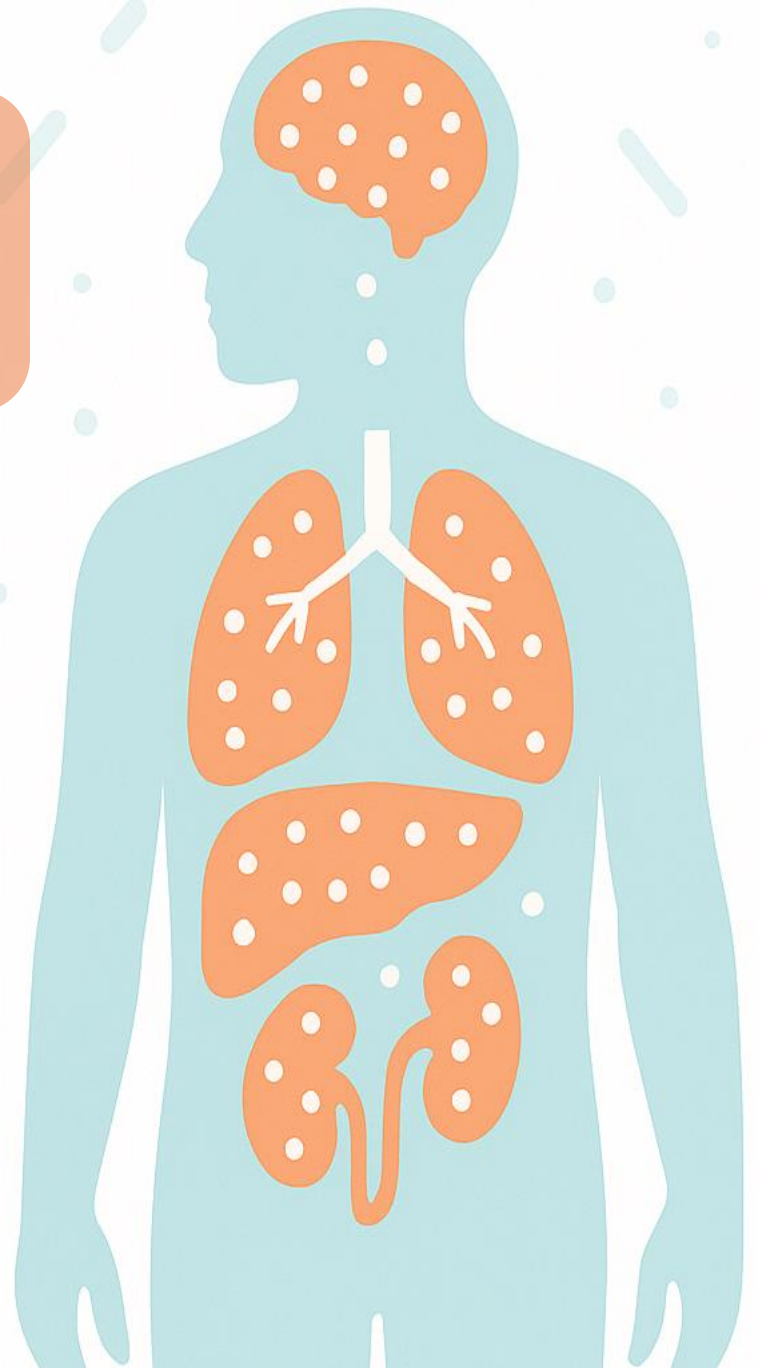


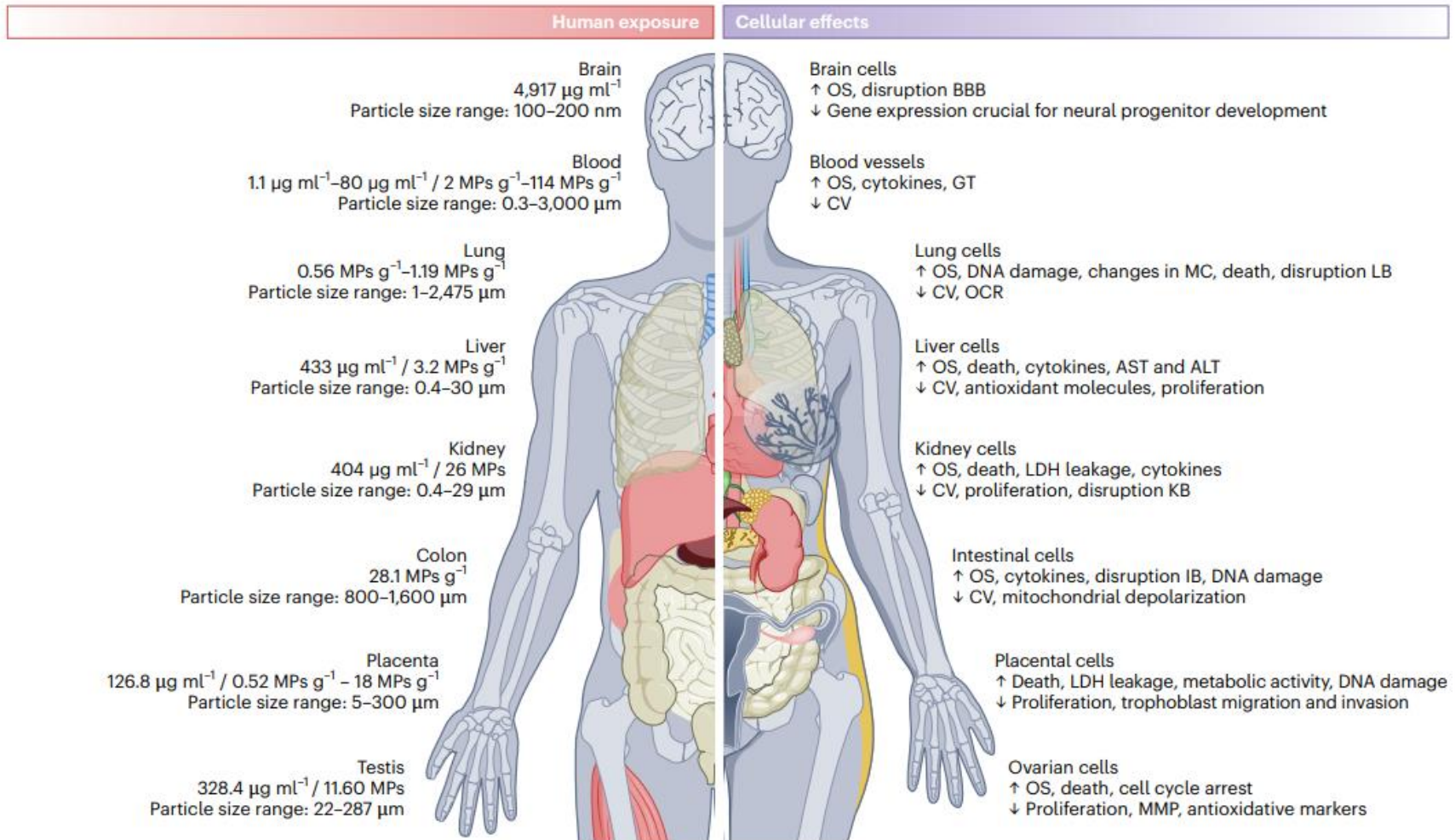
Estimating the internal concentrations of NMPs by PBK model

Ira Wardani, Nur Hazimah Mohamed Nor, Merel Kooi, Albert A Koelmans

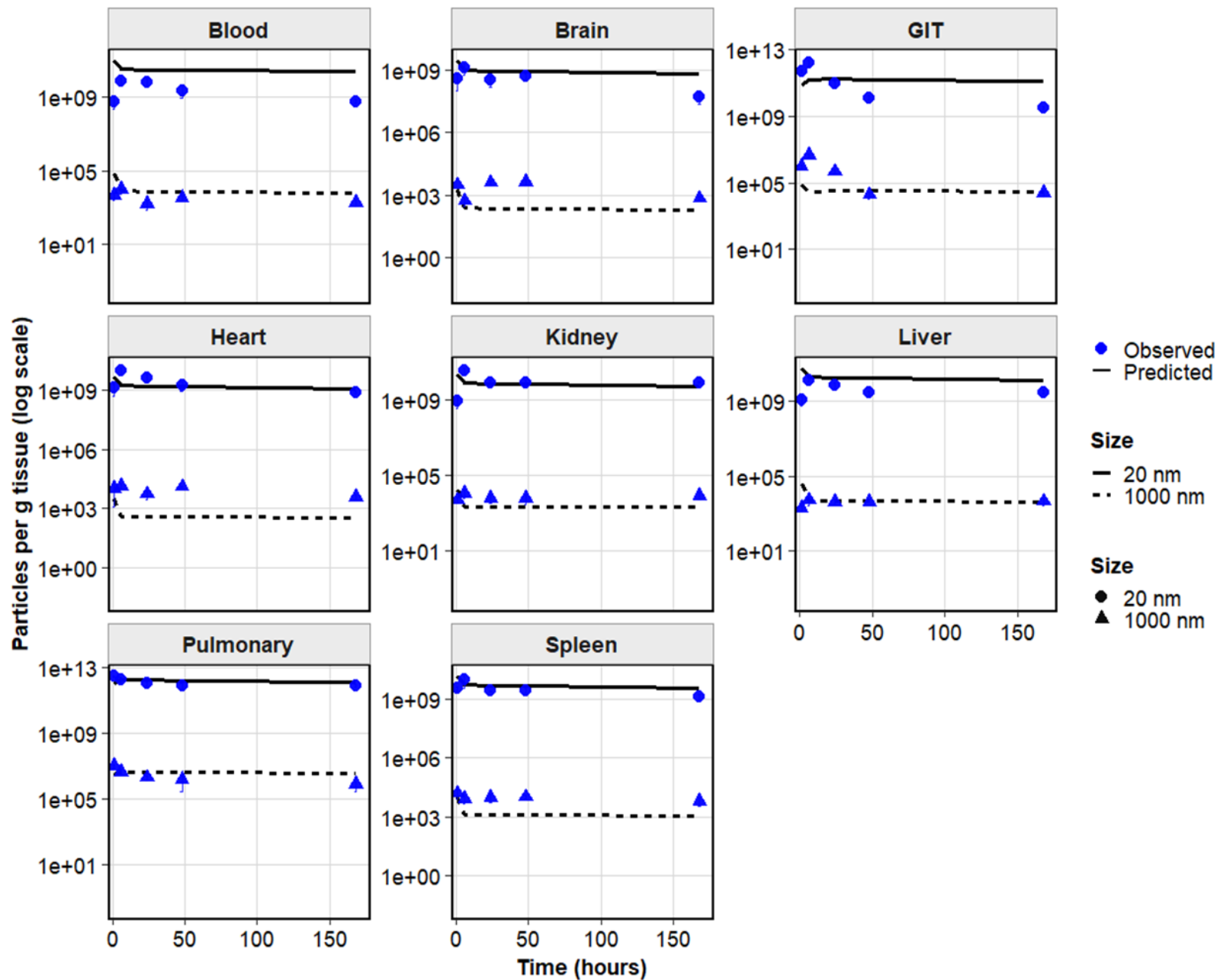
MARII Workshop - Madrid
15-17 Oct 2025



NMPs problem for human health

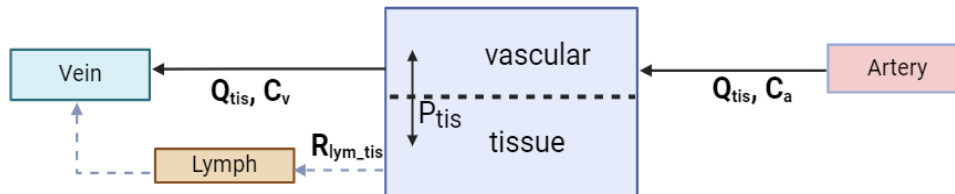


Inhalation PBK model: Predicted vs Observed (20 nm & 1000 nm; log10 $\pm$ SD)



Transport mechanism of NMPs

Perfusion-based PBK model

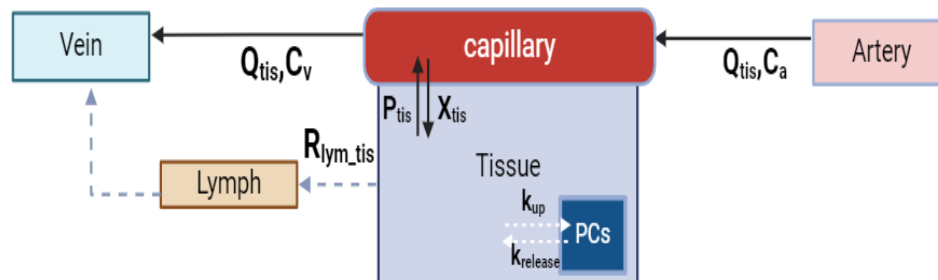


$$\frac{dN_{tis}}{dt} = Q_{tis}(C_a - C_v) - R_{lym_tis}$$

Net flow in the blood

Leakage to the lymph nodes

Diffusion-based PBK model



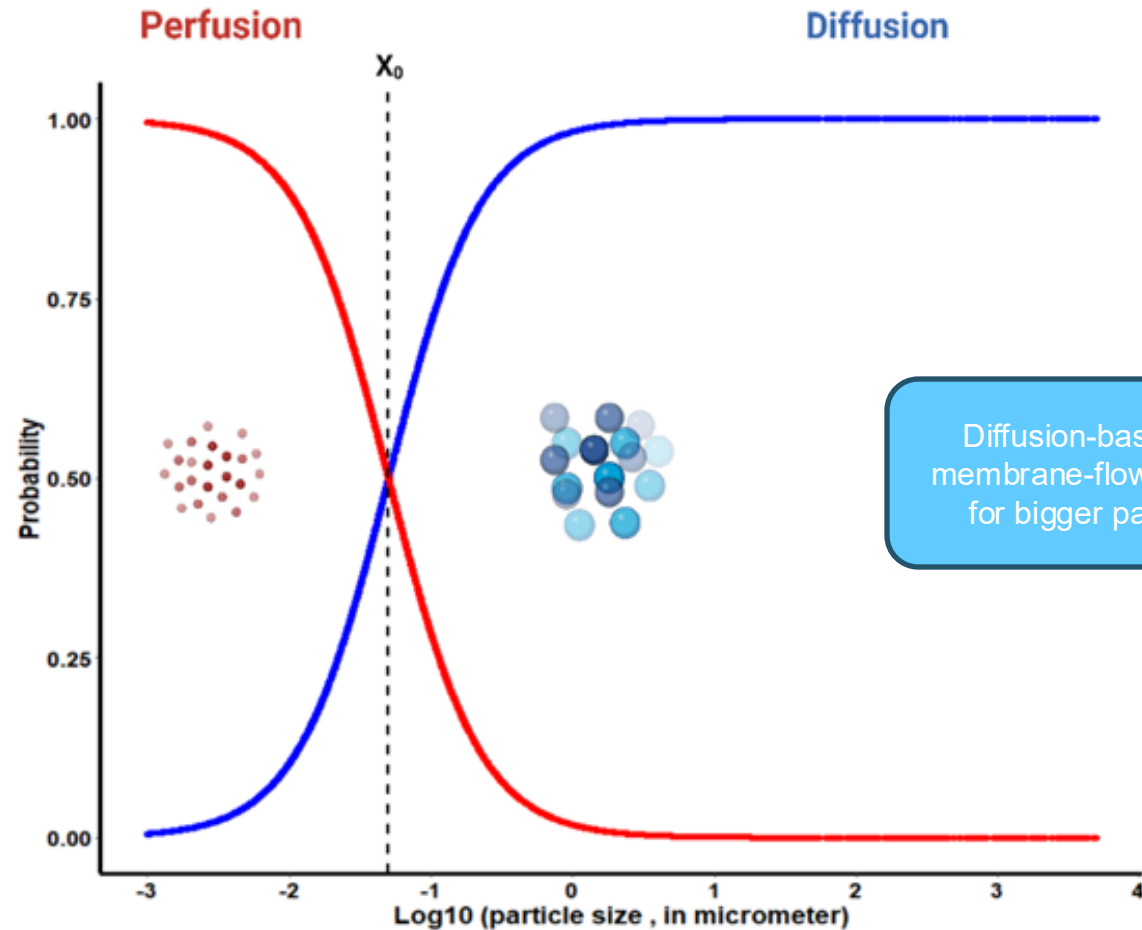
$$\frac{dN_{tis}}{dt} = \chi_{tis} Q_{tis}(C_a - C_v) - k_{up} N_{tis} - k_{release} N_{PC_tis} - R_{lym_tis}$$

Net flow in the blood and cell membranes

Uptake and release by PCs

Leakage to the lymph nodes

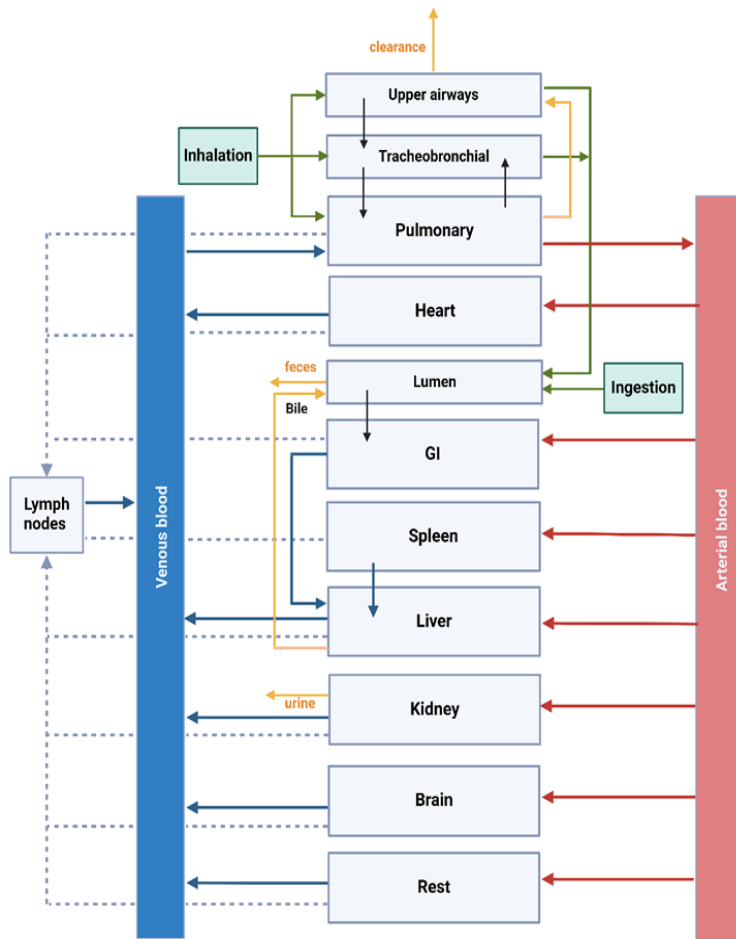
Transport mechanism of NMPs



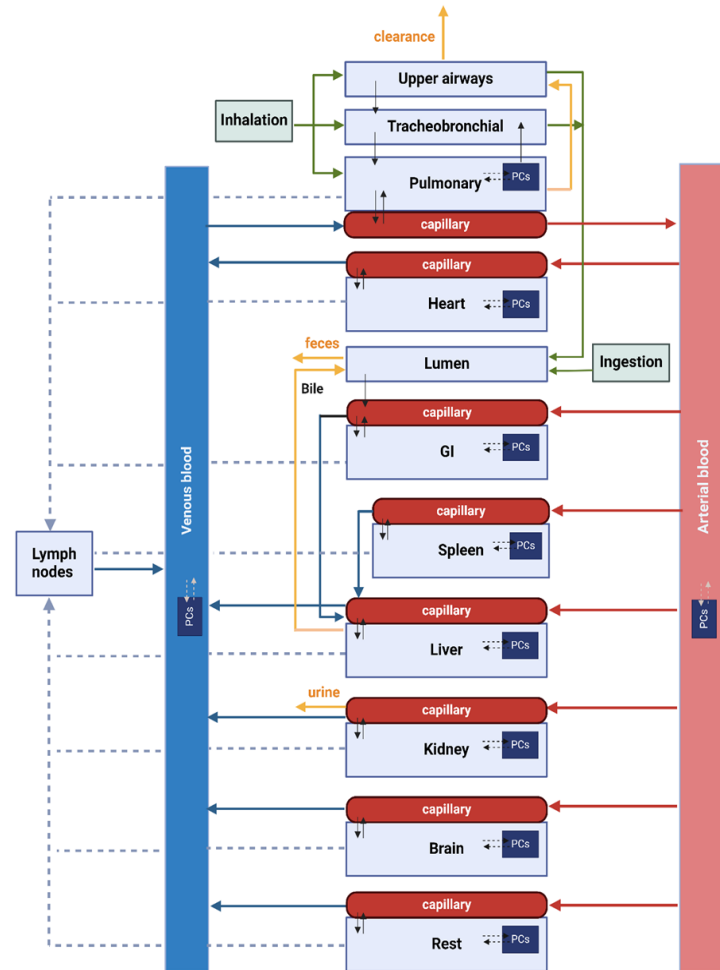
Perfusion-based or
blood-flow limited for
smaller particle

Diffusion-based or
membrane-flow limited
for bigger particle

Physiologically based kinetic model



Perfusion-based



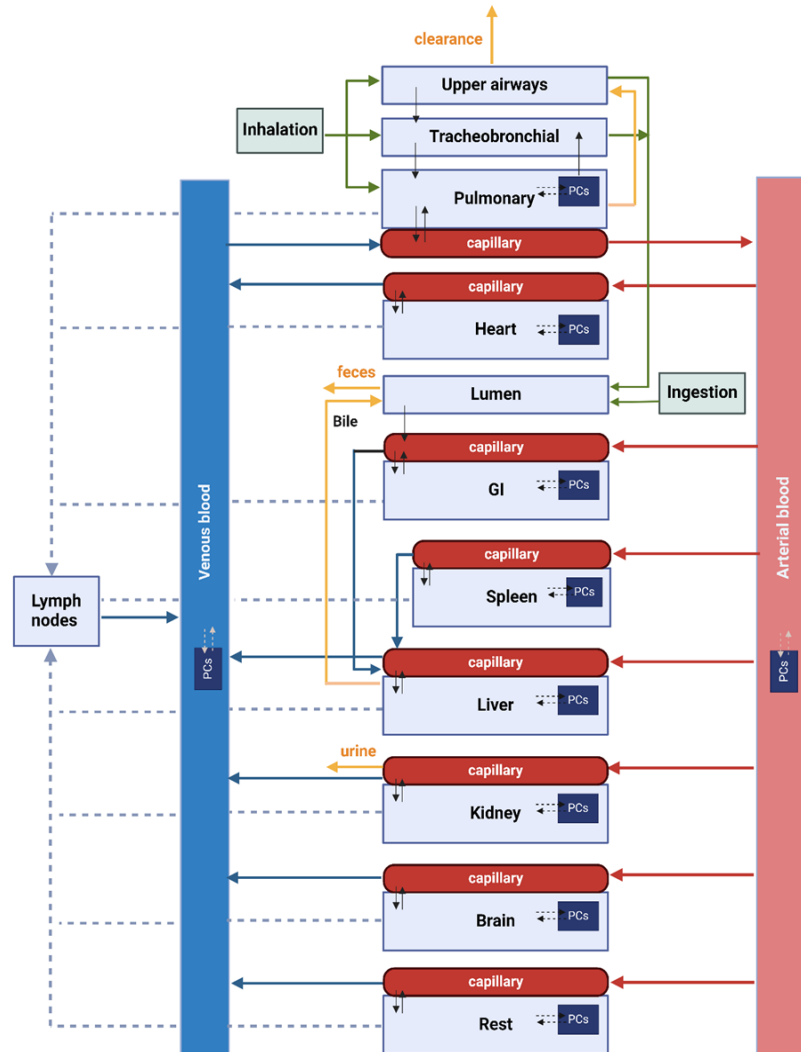
Diffusion-based

Physiologically based kinetic model

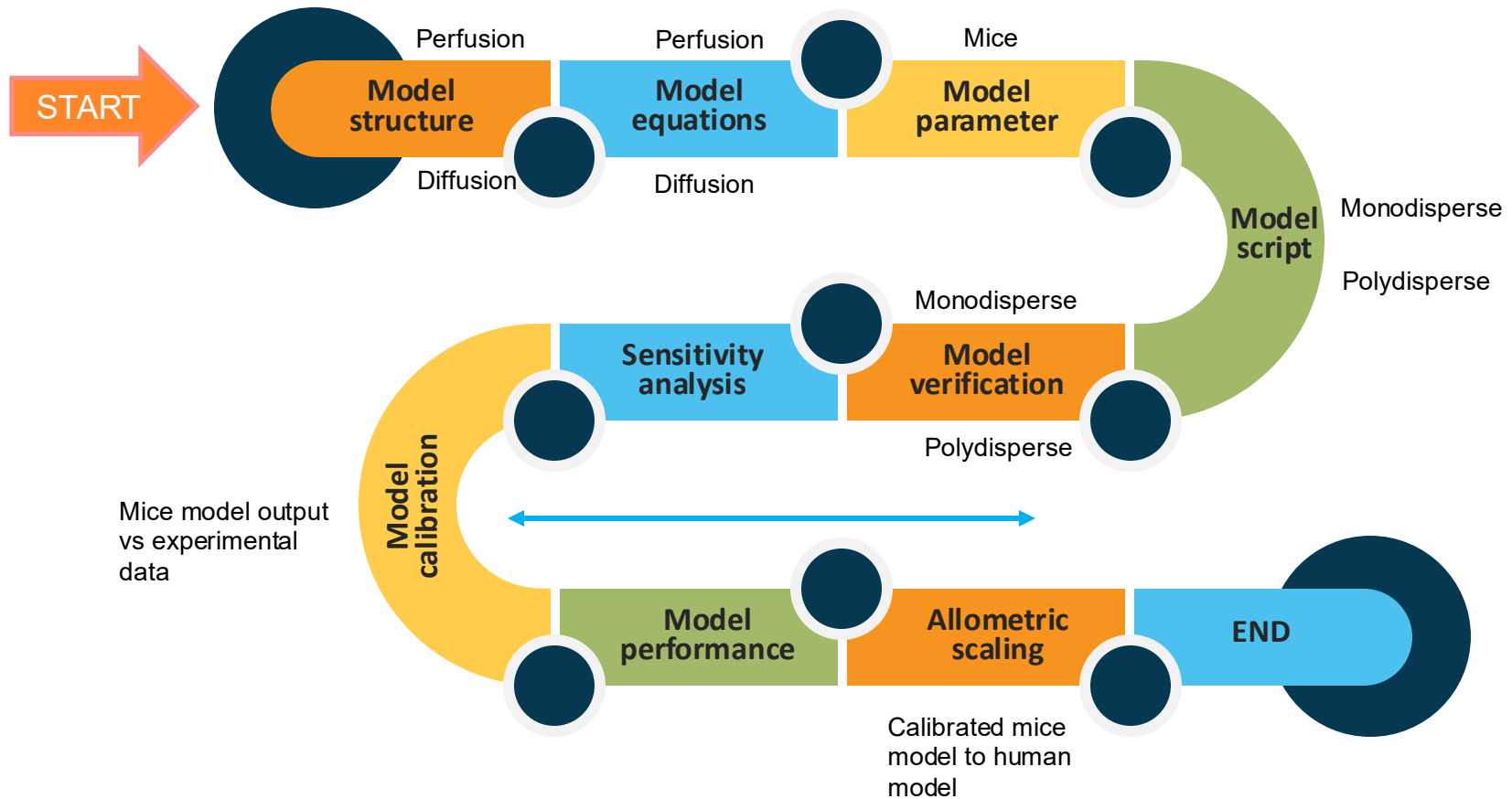


Highlights

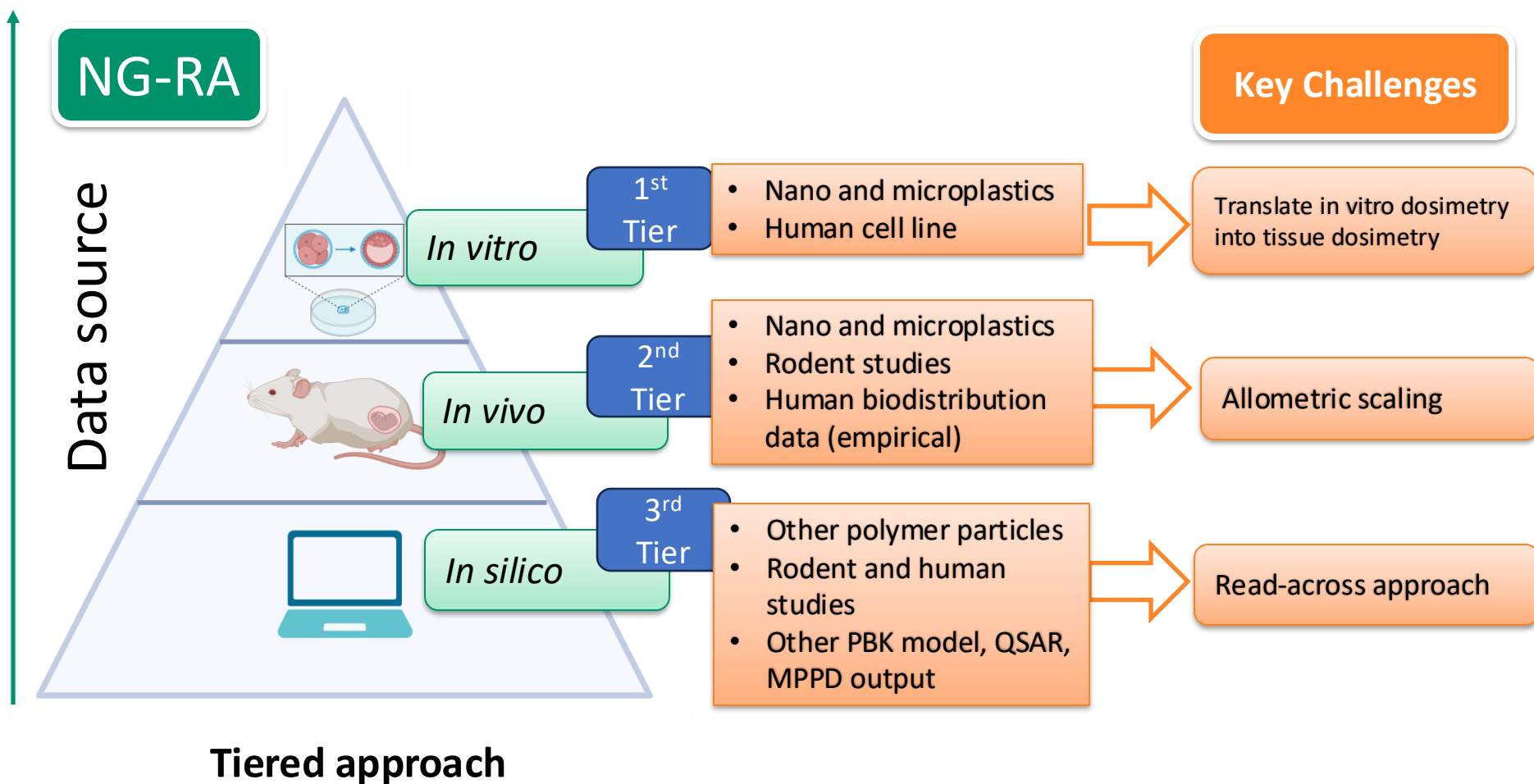
- Particle number as the output unit
- Mice and human model
- Monodisperse and polydisperse
- Size-dependent model parameters
- Inhalation & ingestion exposure



Modeling workflow

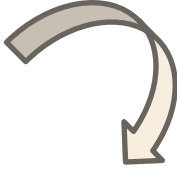
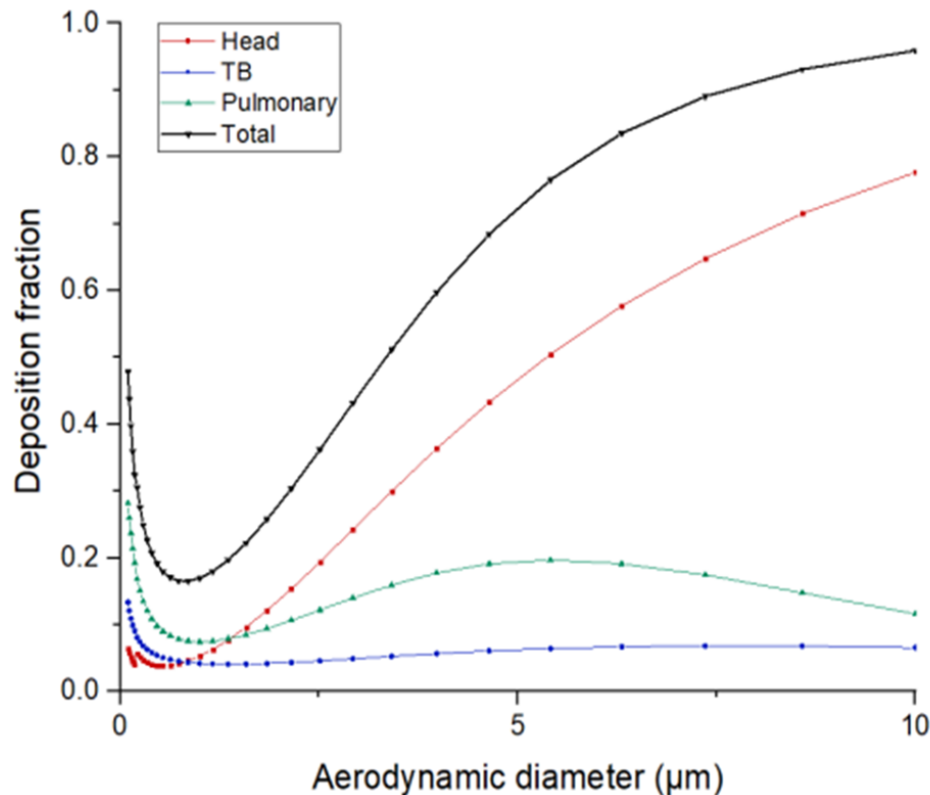


Model parameterization



Size-dependent model parameters

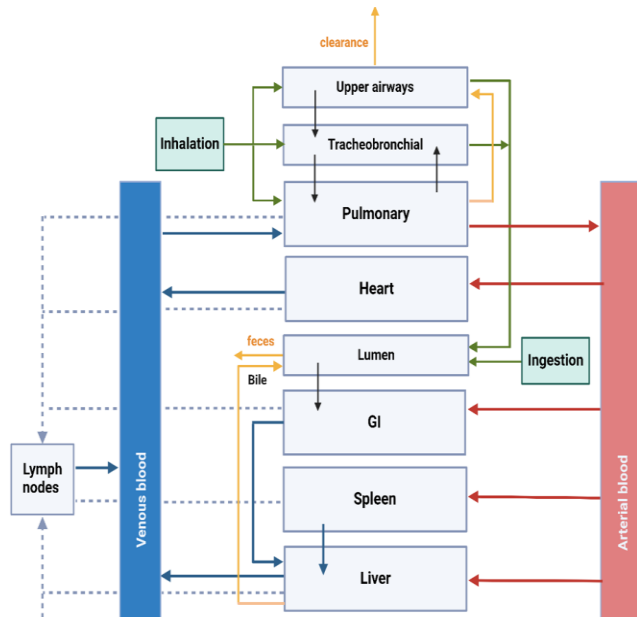
Deposited fraction of MPs in different respiratory region based on MPPD output



region	c0	c1	c2	c3	c4
Pulmonary	0.067587	0.050488	0.366304	-0.12874	-0.23314
Tracheobronchial	0.041681	-0.01254	0.084392	-0.02341	-0.02082
Head	0.038069	0.14931	0.575814	0.26531	-0.2402


$$f(d) = c_0 + c_1 \log_{10}(d) + c_2 [\log_{10}(d)]^2 + \dots + c_K [\log_{10}(d)]^K$$

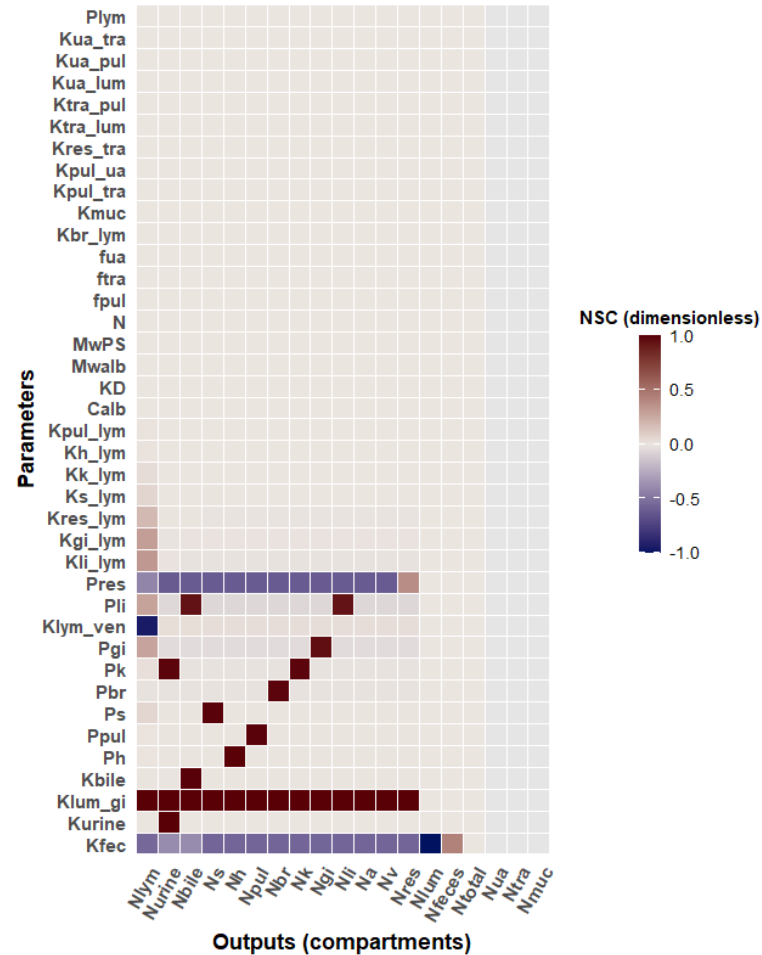
Sensitivity analysis



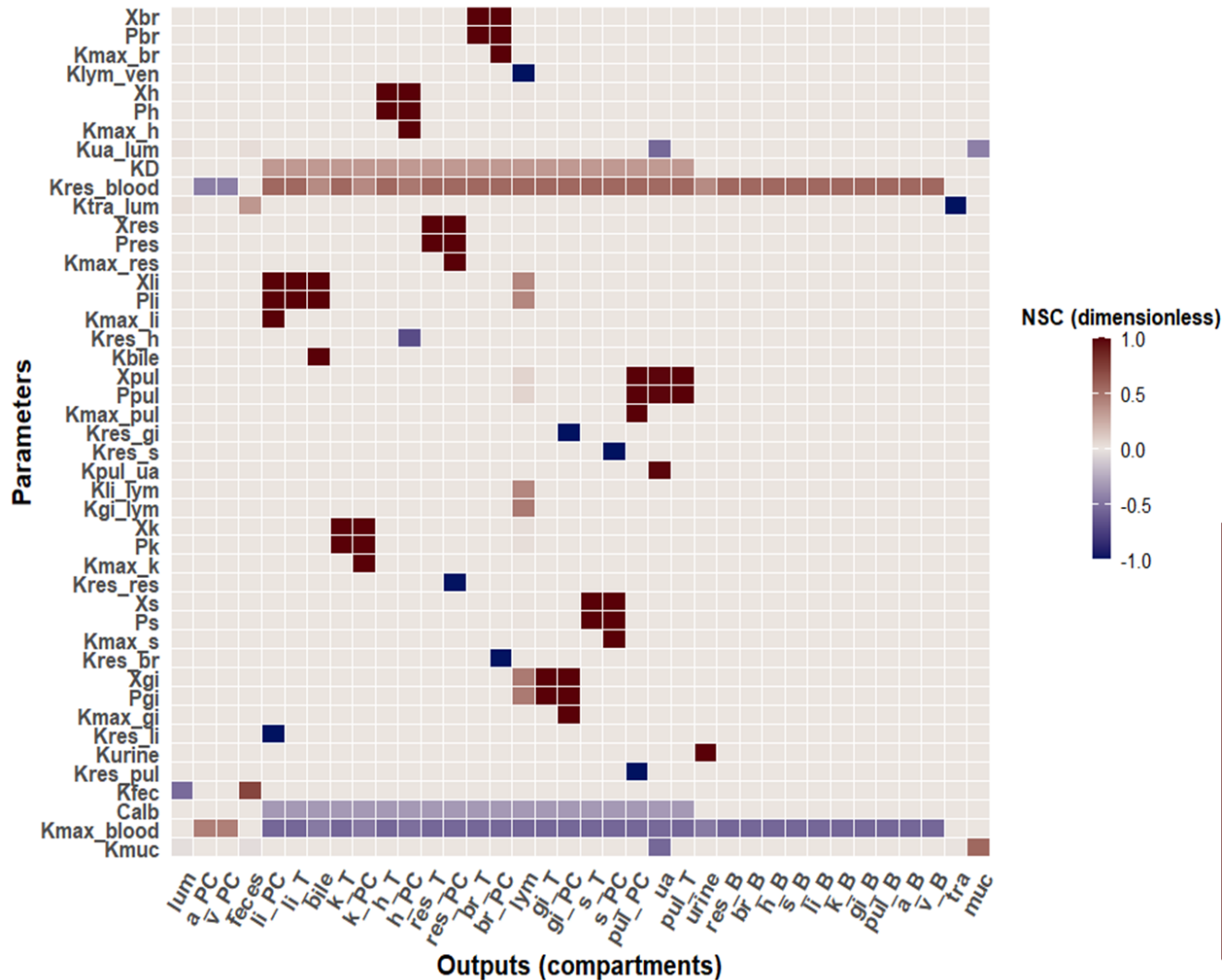
Determine fixed and variable parameters

Normalized Sensitivity Coefficient

Parameter perturbations



Sensitivity analysis



Most sensitive parameters

Perfusion-based model:

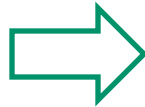
- Kfec
- Klum_gi
- Pres

Diffusion-based model:

- Kmax_blood
- Kres_blood
- KD
- Calb

Model calibration

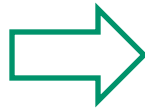
Inclusion
criteria for
experimental
dataset



- Time-series biodistribution data (in vivo) for rodents (mice or rats)
- Exposure routes are defined
- Experimental design information
- Particle characteristics information are provided.
- Standard deviations are provided
- Dose and biodistribution output can be converted as #/gr tissue



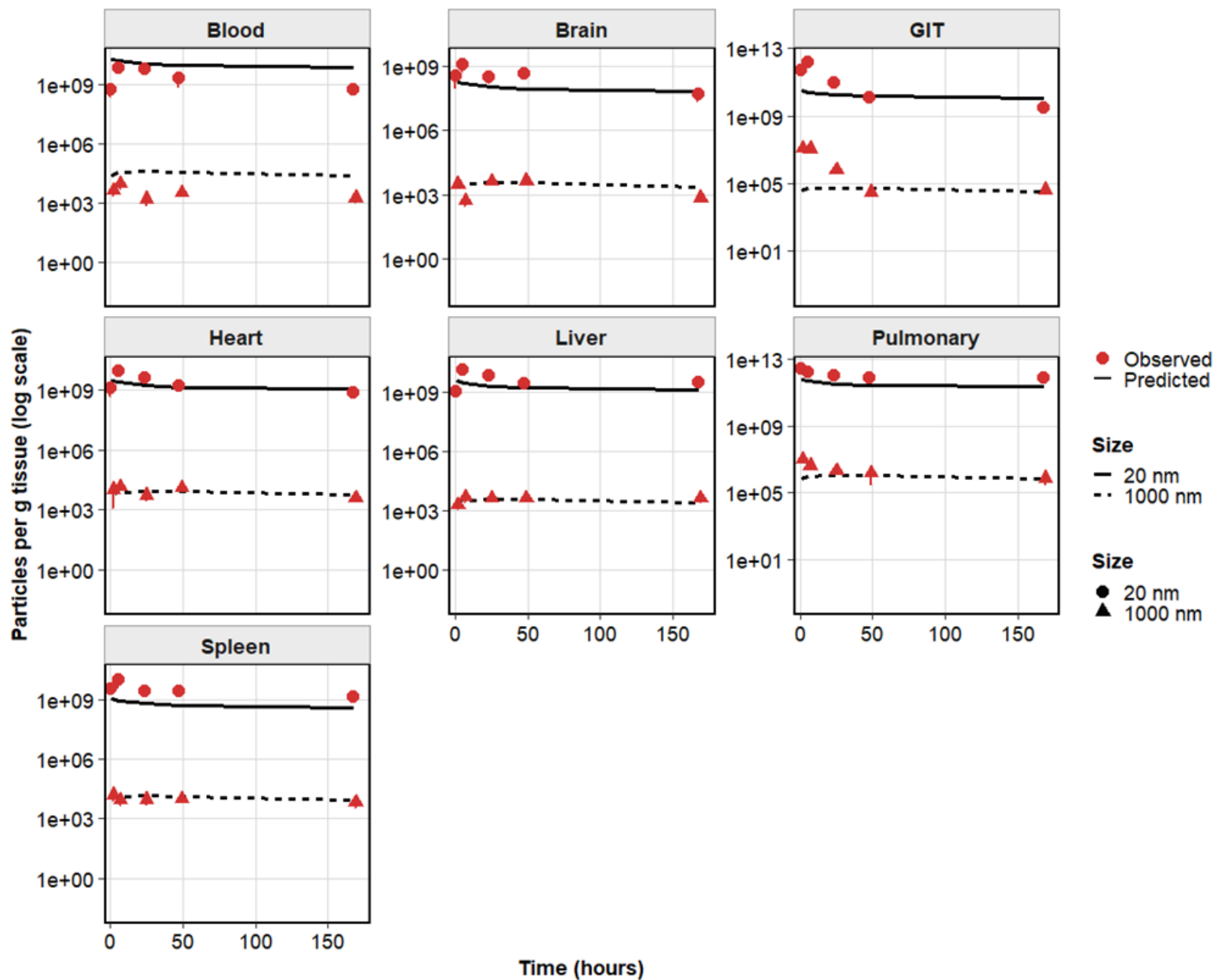
Challenges



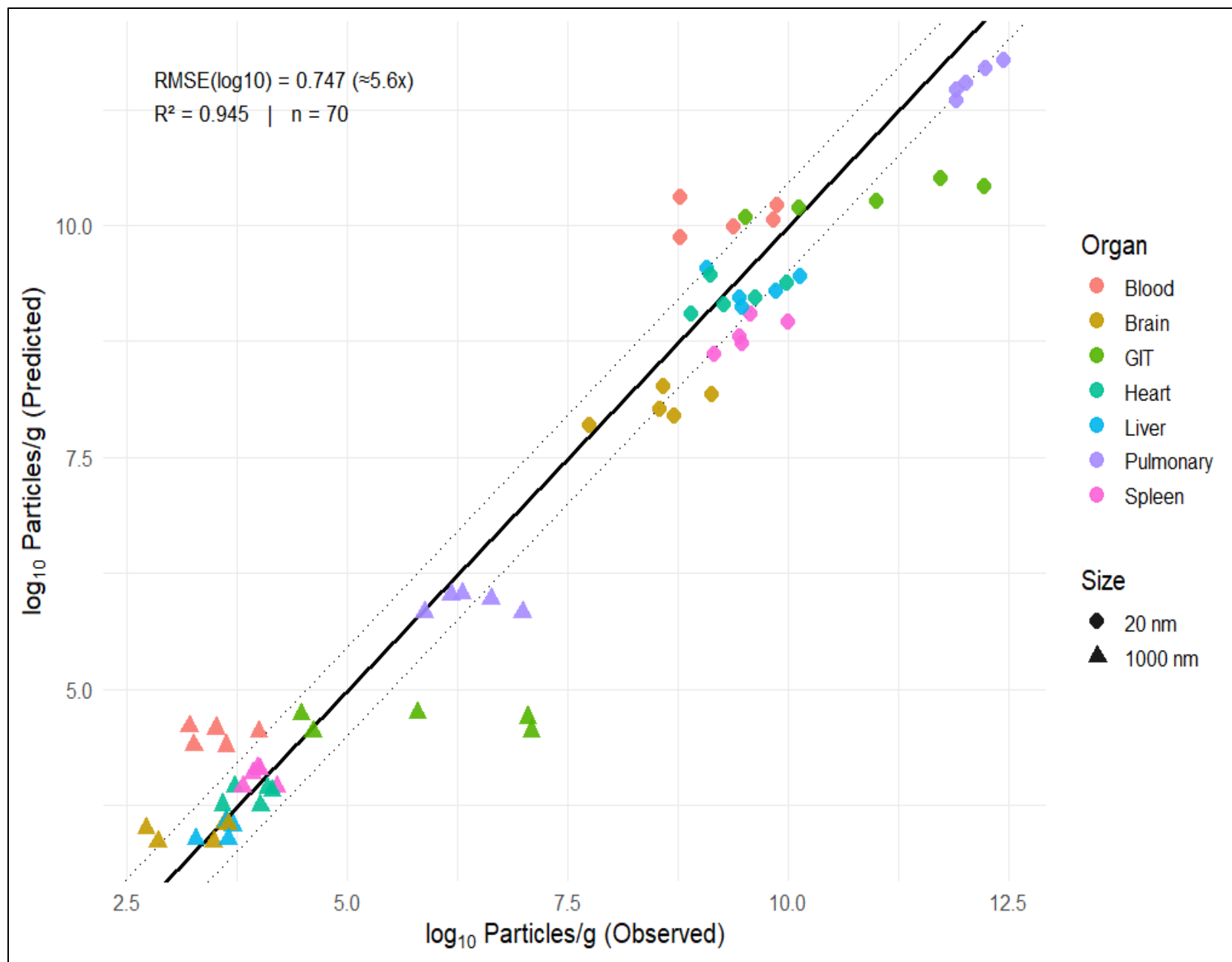
- No biodistribution data from pristine MPs
- Surface characteristics might affect the uptake of NMPs

Perfusion-based

Inhalation PBK model: Predicted vs Observed (20 nm & 1000 nm; $\log_{10} \pm \text{SD}$)

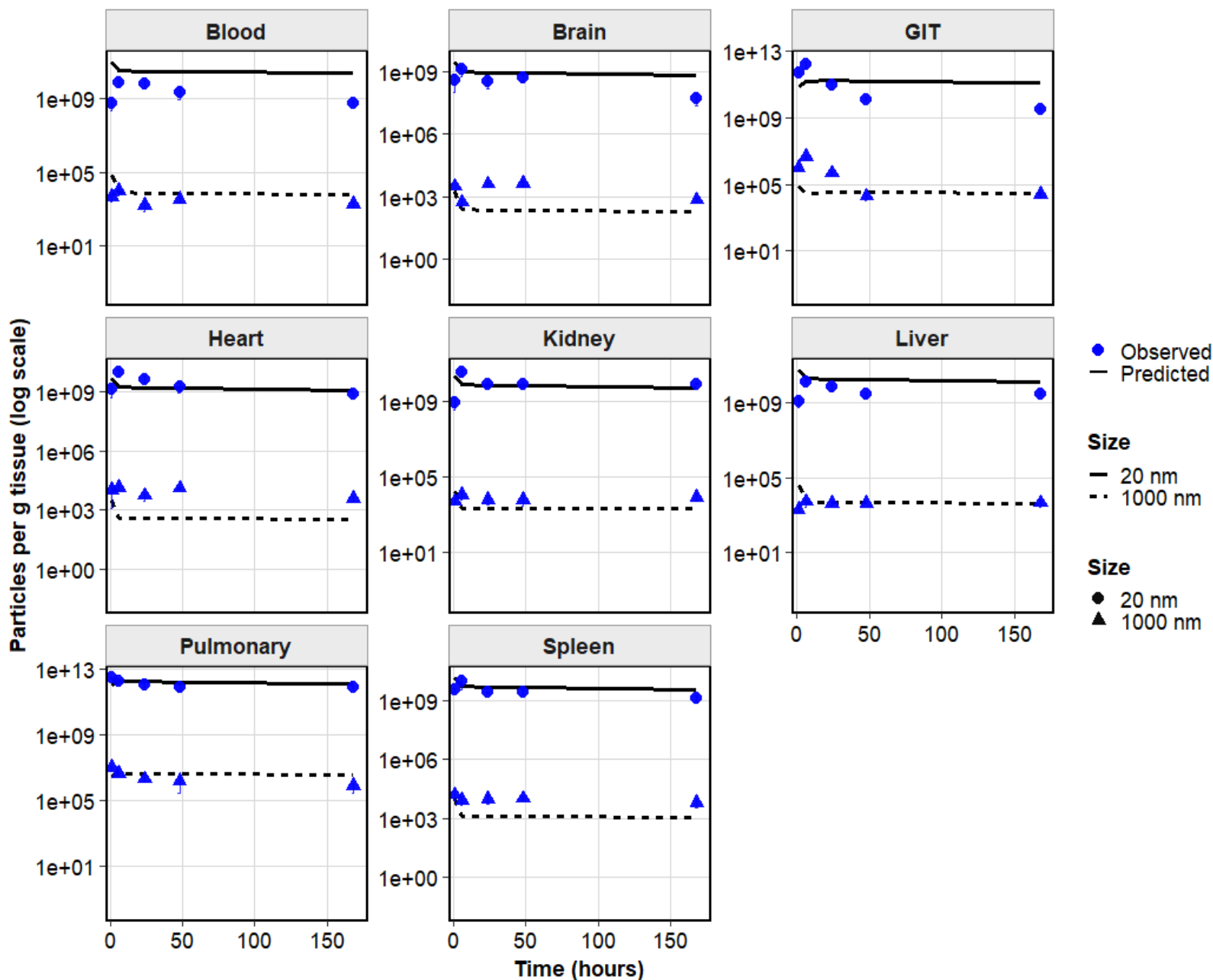


Perfusion-based

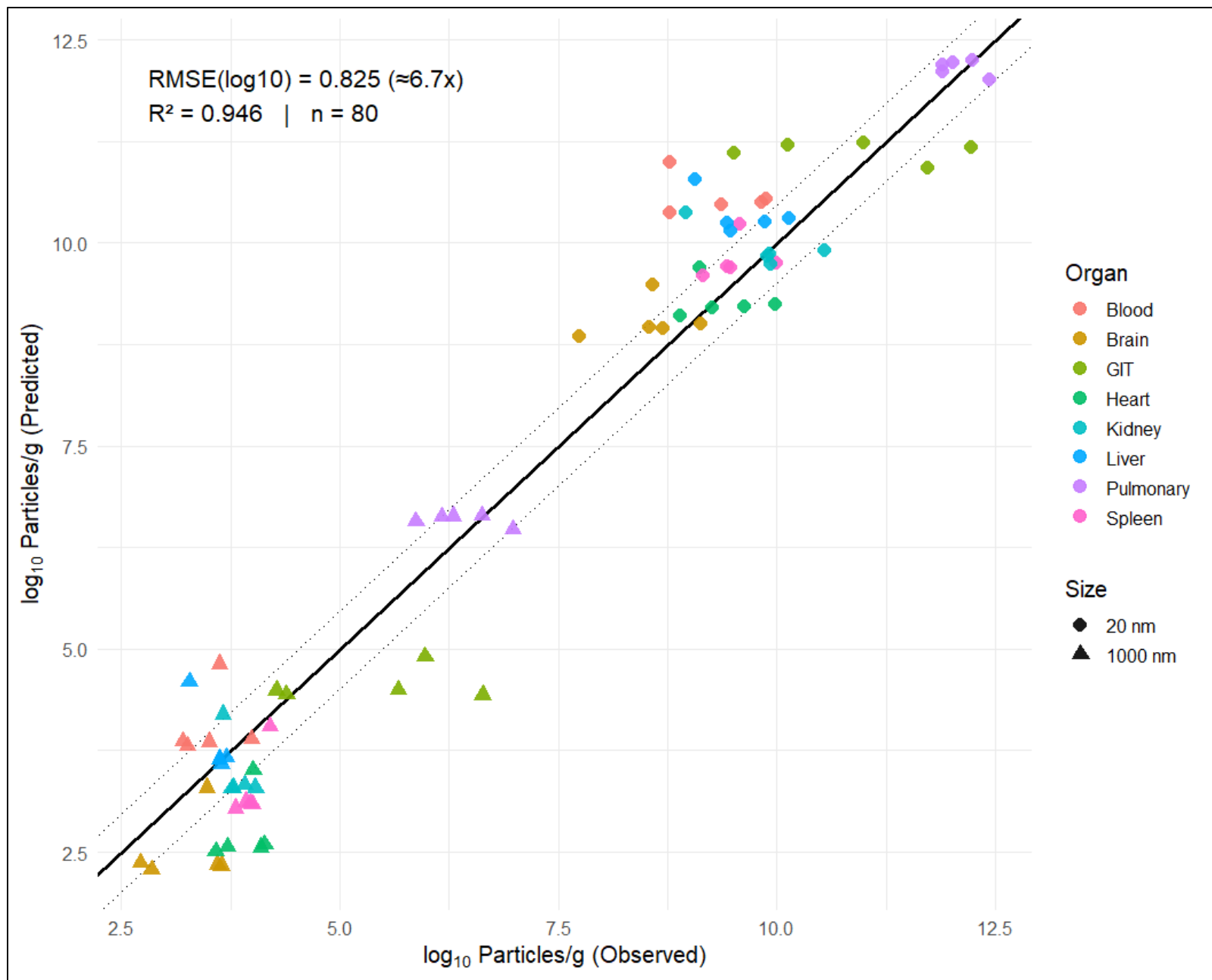


Diffusion-based

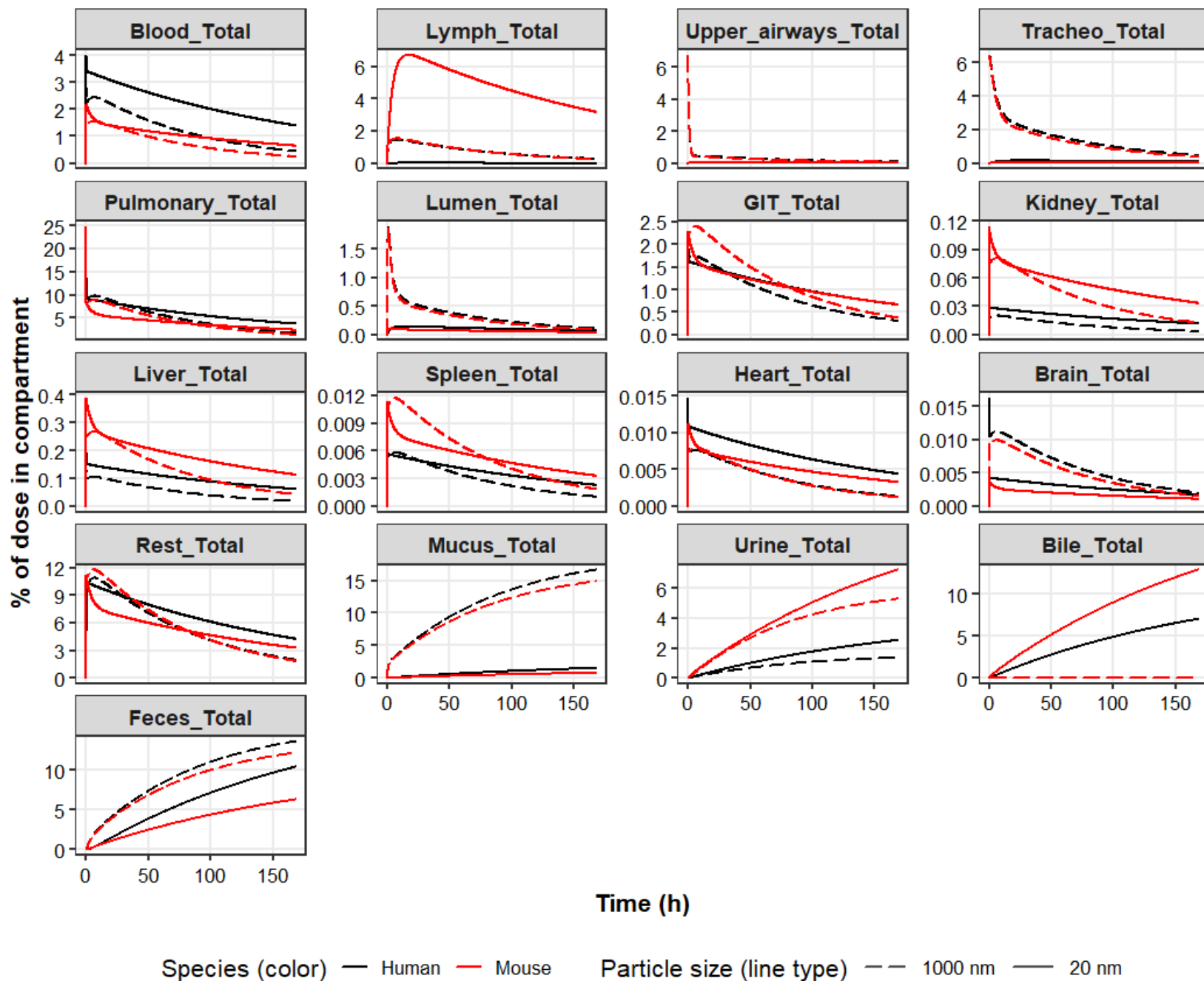
Inhalation PBK model: Predicted vs Observed (20 nm & 1000 nm; $\log_{10} \pm \text{SD}$)



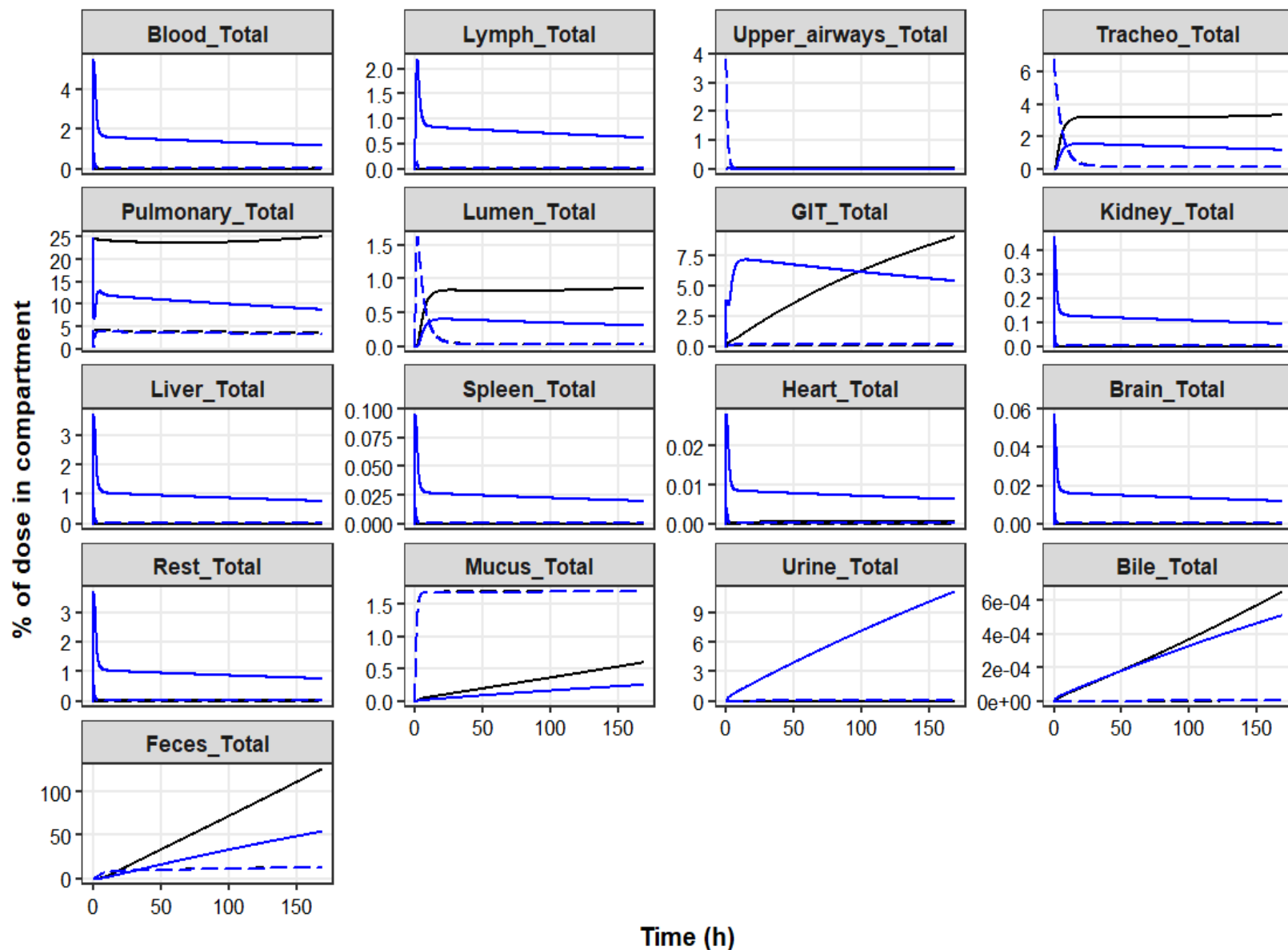
Diffusion-based



PBPK comparison (Inhalation route): % dose vs time

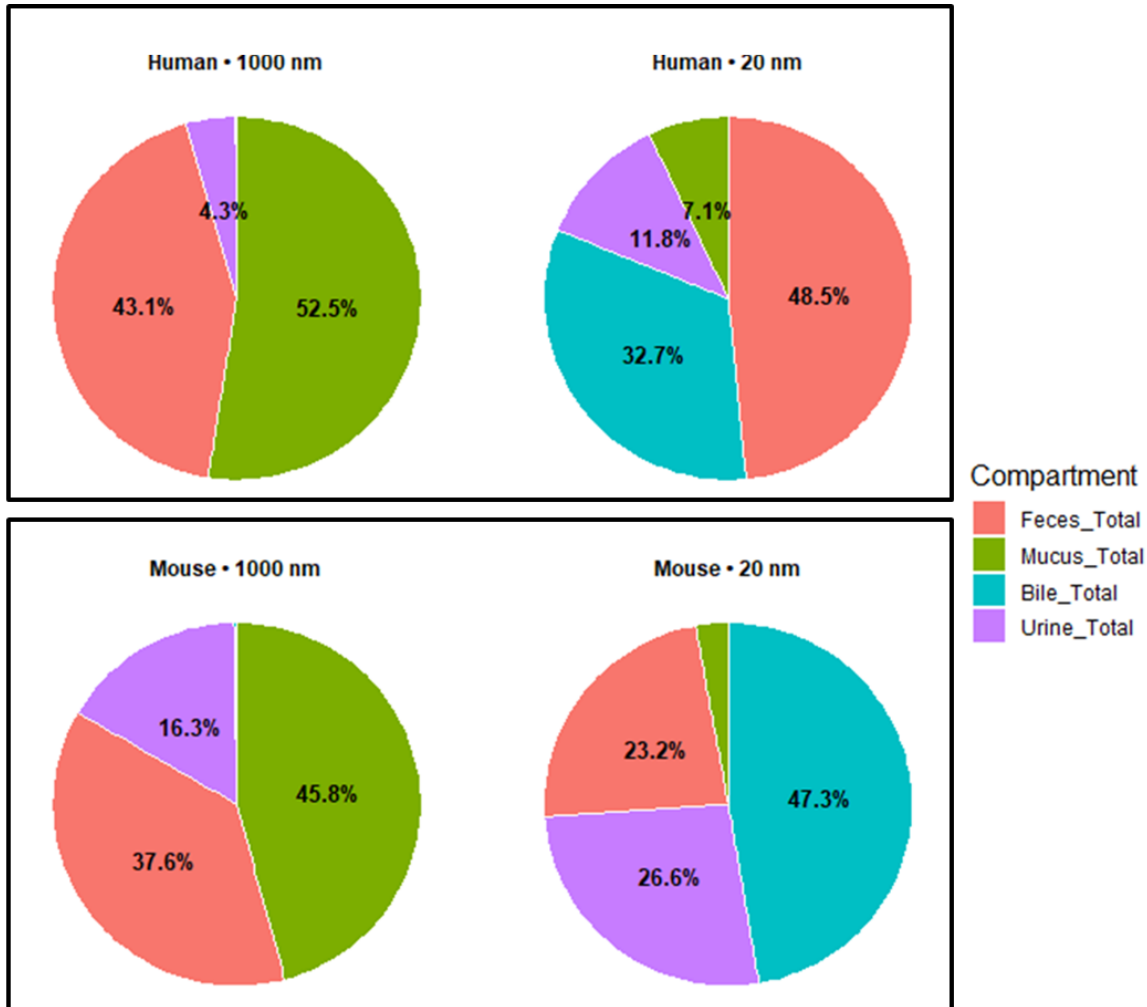


PBPK comparison (Inhalation route): % dose vs time



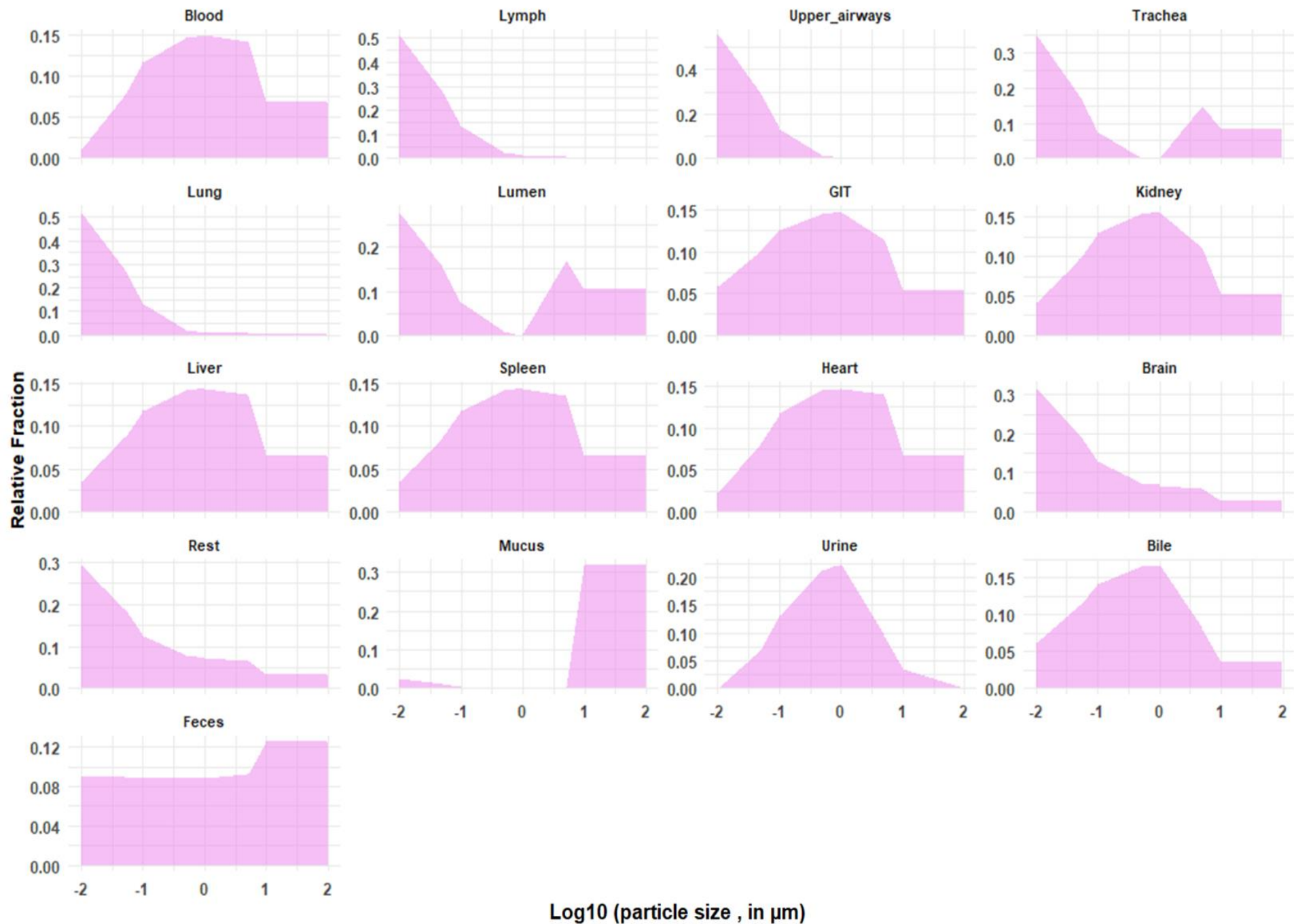
Species (color) — Human — Mouse Particle size (line type) — — 1000 nm — 20 nm

Excretion profile by species and particle sizes

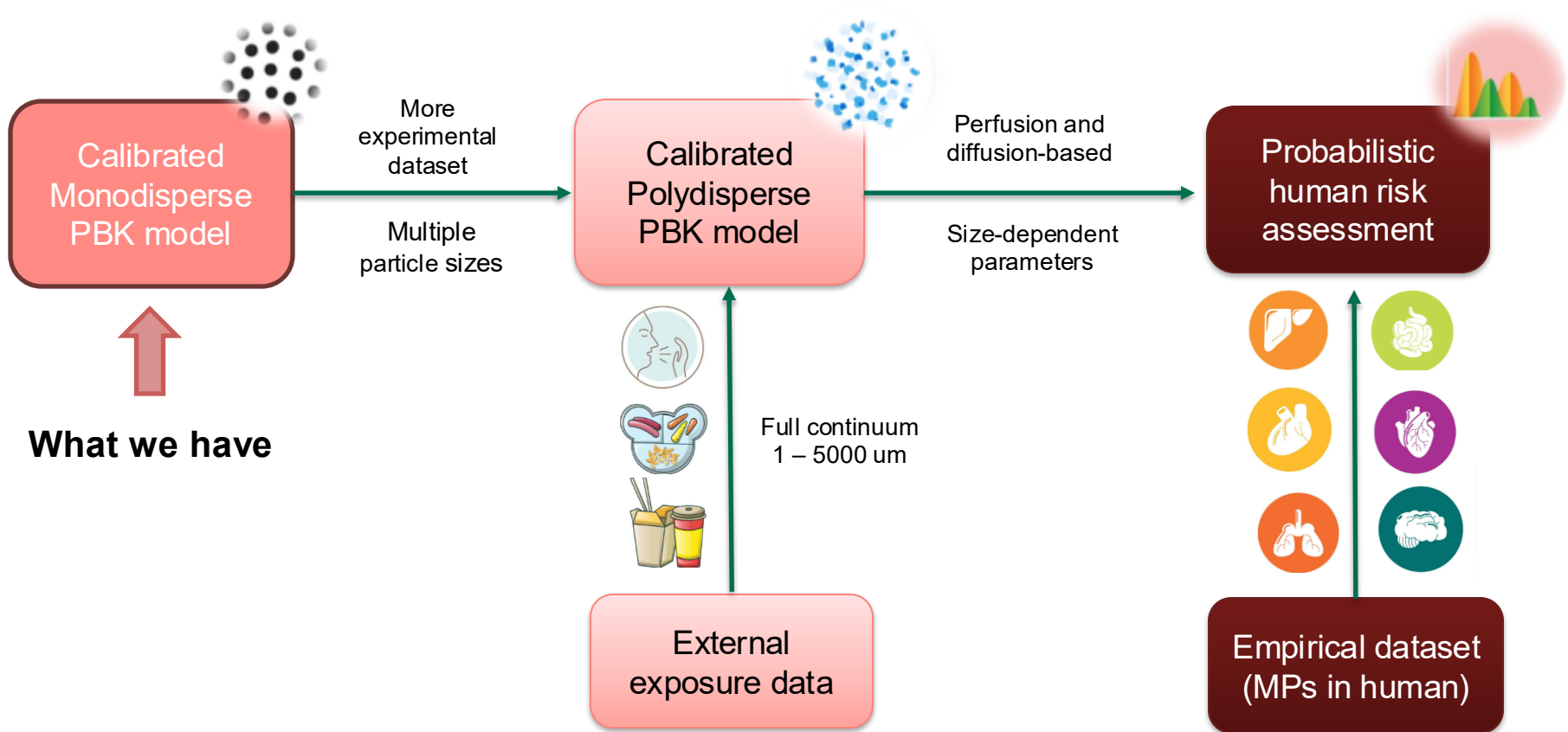


- Bigger particles from inhalation route are mostly excreted through mucus and feces for both species
- Smaller particles are mostly excreted through feces and bile in human
- Smaller particles are mostly excreted through bile and urine in mice

Hybrid Model: Size Distribution for Each Compartment (Normalized, log10 Scale)



Next “Scenario”





Ellen Besseling



Paula Redondo Hasselerharm



Georgiana Amariel



Bart Koelmans



Merel Kooi



Svenja Mintenig



Sven Frei



Noël Diepens



Nur-Hazimah Mohamed Nor

Microplastic Lab

by all of us

www.microplasticlab.com



Vera de Ruijter



Yanning Qiu

Thank you!

Aquatic Ecology & Water Quality Management Group



WAGENINGEN
UNIVERSITY & RESEARCH



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Margherita Barchiesi



Virginia Gálvez Blanca



Annie Hunnestad



Derk van Grootheest



Dung Nguyen



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Ira Wardani



Yutong Guo



Yvette Mellink